Journal of Surgical Oncology 1999;70:64–67

Oliguria, an Unusual Presentation of Primary Signet Ring-Cell Adenocarcinoma of the Urinary Bladder: A Case Report and Review of the Literature

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Adenocarcinomas represent approximately 2% of primary bladder epithelial malignancies. Of these, the signet ring-cell variant is the rarest form. We report such a case, with the unusual presentation of oliguria, including radiologic and histopathologic findings. The current literature is reviewed.
J. Surg. Oncol. 1999:70:64–67.

KEY WORDS: bladder cancer; renal failure; urinary obstruction

INTRODUCTION

In 1955, Saphir [1] first described signet ring-cell adenocarcinoma of the urinary bladder as a distinct entity. Approximately 2% of primary bladder epithelial malignancies are adenocarcinomas, with the signet ring-cell variant being the rarest form [2]. Herein, we review the current literature and report a case, with its radiologic and histopathologic findings.

CASE REPORT

An 84-year-old Caucasian male was referred to our Urology Clinic on January 29, 1997, with a 3-week history of oliguria and progressive lower urinary tract irritative symptoms. There was no history of hematuria or urinary incontinence. The patient also complained of anorexia, fatigue, and constipation of 3 months' duration. He had not experienced weight loss or bone tenderness. Past medical history included hypertension, myocardial infarction (1991), and benign prostatic hyperplasia, for which a transurethral resection of the prostate was performed in 1971. Digital rectal examination revealed a flat prostate with marked induration of the rectal wall circumferentially. Mild pitting edema of the lower extremities was noted.

The patient was mildly anemic [hemoglobin 114 g/l (normal 140–175 g/l), hematocrit 0.33 (normal 0.42–0.50)] with normal serum electrolytes, liver function tests, and coagulation studies. Serum prostate-specific antigen (PSA) was also within normal limits [3.3 μg/l (normal <4.0 μg/l)]. Blood urea nitrogen (BUN) was elevated [25.7 mmol/l (normal 2.9–8.2 mmol/l)], as was the serum creatinine [313 μmol/l (normal 70–125 μmol/l)]. Urine analysis and cultures were negative. Urine cytology revealed the presence of atypical cells. Renal ultrasonography demonstrated moderate bilateral hydronephrosis with preservation of the renal parenchyma. Cystoscopic evaluation revealed a patent bladder neck and no obvious mucosal lesions. Bullous edema was observed on the bladder floor and posterior wall, suggestive of an invasive process. The ureteric orifices could not be identified. Biopsy sampling of the bladder (Figs. 1, 2) revealed diffuse infiltration of the lamina propia with a population of non-cohesive, round to polygonal tumor cells. Cells were frequently characterized by eccentric nuclear positioning and the presence of a mucosubstance-rich [positive for periodic acid-Schiff (PAS) after diastase and mucicarme staining], glassy cytoplasm or clear vacuole conveying a signet ring configuration. Nuclei had a finely dispersed chromatin and small, distinc-

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Accepted 5 September 1998

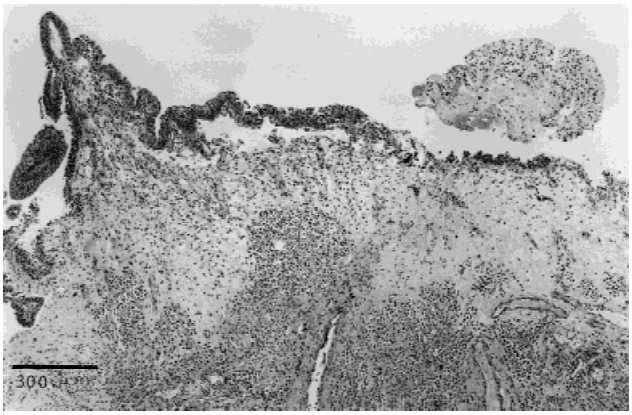

Fig. 1. Bladder biopsy revealing a diffuse infiltrate of neoplastic cells within lamina propria with overlying normal urothelium. Note the presence of associated edema and congestion in the suburothelial region. Hematoxylin-eosin, 25× original magnification.

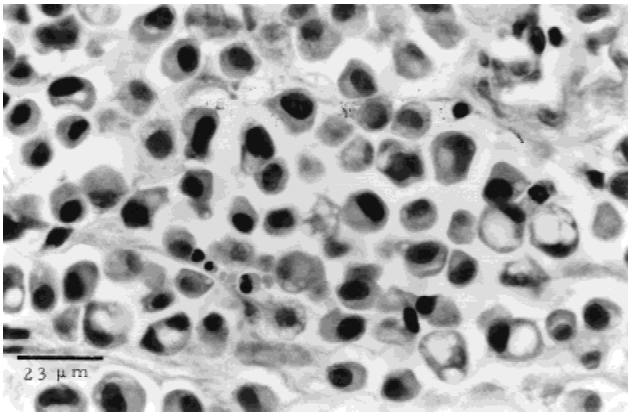

Fig. 2. Noncohesive infiltrate of tumor cells with eccentric nuclear positioning and mucin-positive intracytoplasmic vacuoles characteristic of poorly differentiated signet ring adenocarcinoma. Hematoxylin-eosin, 400× original magnification.

tive nucleoli. Tumor cells were strongly immunoreactive for cytokeratin AE1-AE3 (Boehringer-Mannheim, Indianapolis, IN; dilution 1:800) and carcinoembryonic antigen (CEA) (Dakopatts, Mississauga, Canada; dilution 1: 6,000) but negative for PSA (Dakopatts, dilution 1: 5,000). Edema and marked congestion were present in the suburothelial region, conveying a micropolypoid configuration on the luminal aspect. There was no evidence of urothelial dysplasia or neoplasia, intestinal metaplasia, cystitis cystica, or cystitis glandularis.

A right percutaneous nephrostomy tube was inserted on January 30, 1997. BUN and serum creatinine values began to fall immediately thereafter, reaching a nadir on the third postoperative day (5.0–6.5 mmol/l and 110–120 μmol/l, respectively). Serial measurements of serum alkaline phosphatase were normal, while those of CEA were elevated [12.6–12.8 μg/l (normal <3.0 μg/l)]. Chest radiograph and bone scan were both normal. Computed tomography (Fig. 3) demonstrated circumferential bladder wall thickening to 2 cm. Diffuse fat stranding in the retroperitoneum obliterated fat planes, thus limiting assessment of tumor extension and invasion. Colonoscopy revealed external compression of the rectum at 10 cm. Biopsies demonstrated clusters of poorly differentiated signet ring-cell adenocarcinoma with sparing of the mucosa, consistent with metastatic involvement. Gastroscopy and biopsies of the stomach were negative. After discussing the treatment options with the patient, such as cystectomy, urinary diversion, fecal diversion, radiotherapy, or chemotherapy, he elected not to undergo any further treatment. He was discharged from hospital on March 19, 1997, with the right percutaneous nephrostomy tube to straight drainage and died on April 17, 1997. Autopsy permission was not granted.

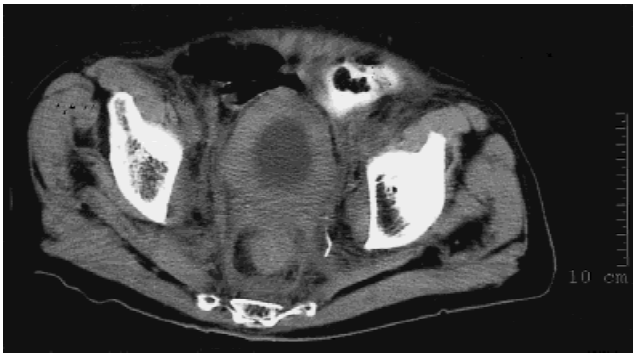

Fig. 3. Single cut from an axial computed tomographic scan of the pelvis (unenhanced due to the elevated creatinine), demonstrating circumferential bladder wall thickening. The wall thickening was most pronounced near the bladder dome. Also seen is retroperitoneal fat stranding, part of a diffuse process likely secondary to renal failure.

DISCUSSION

Primary signet ring-cell adenocarcinoma of the urinary bladder is rare, with approximately 70 reported cases in the literature [3]. Despite these reports, this entity remains inadequately defined [4]. Saphir [1] originally described signet ring cells as present ''in a substantial number.'' Other descriptions have referred to these cells as being the ''predominant'' [5] or ''primary'' [6] cell type. Such cases may have had a urothelial (transitional cell) malignant component associated with the signet ring carcinoma [6,7]. Grignon et al. [4], using the definition of tumors with the presence of individual signet ring cells permeating the bladder wall (a diffuse signet ring-cell component) in a linitis plastica fashion, excluding a papillary or invasive urothelial carcinoma component, cited only 12 primary signet ring-cell carcinomas out of 76 pure adenocarcinomas of the urinary bladder. In our review of the literature, less than 25 documented cases with the aforementioned definition were found.

The cell of origin for primary adenocarcinoma of the urinary bladder is unknown [6]. It has been postulated to (1) derive from the native urothelium overlying tumors

[8]; (2) be columnar epithelial cells in rests of cloacal origin in the urachus or bladder wall [9,10]; (3) be glandular metaplastic cells in Brunn's urothelial nests [1,9]; (4) be mucin-secreting cells of cystitis glandularis [1,10]. The metaplastic potential of the urothelium has been well described [2], as either intestinal metaplasia or cystitis glandularis [4]. However, few cases demonstrating transition from these lesions to adenocarcinoma have been documented [11]. This is supported in the literature: among 24 cases with a pure diffuse signet ring-cell tumor, none showed either cystitis glandularis or intestinal metaplasia [1,4,8]. Metaplastic transformation of a urothelial carcinoma has also been reported [6]. Signet ring-cell adenocarcinoma has also been documented to occur in the stomach [12], gallbladder [13], cystic duct [14], ileocecal valve [15], urachus [16], and prostate [17,18] and with ileocystoplasty [19]. Its presence in the bladder, as mentioned previously, is uncommon and tends to be metastatic rather than a primary lesion.

The usual clinical presentation of primary signet ring-cell adenocarcinoma of the bladder does not differ significantly from that of other bladder malignancies. Average age at diagnosis is comparable with that reported for adenocarcinoma of the bladder in general. They most frequently arise in the sixth decade of life and have a male preponderance [4,6]. Hematuria and irritative symptoms are the most common presenting complaints [4,6]. Other symptoms include constipation, fecal incontinence, and back pain. There appears to be no correlation between the duration of symptoms and the stage of disease [6]. Because it is silent and extremely aggressive, a signet ring-cell tumor is usually diagnosed late and outcome is often poor [3,20]. Patients tend to present with advanced disease, with 65% of all cases being stage D [4]. It is important to distinguish between tumors with a diffuse or linitis plastica-like architecture from those in which other adenocarcinomatous patterns are associated with the signet ring cells as the former have a significantly worse prognosis [4].

Our case documented here is atypical in various aspects. The patient presented in his ninth decade of life with the unusual symptom of oliguria. To our knowledge, this is the first reported case of signet ring-cell adenocarcinoma that has presented in this fashion. Metastatic evaluation detected no distant presence of tumor. There was, however, invasion of tumor into the rectum, making it a stage D lesion. Rectal biopsy sampling revealed a few clusters of poorly differentiated signet-ring adenocarcinoma cells at the interface of muscularis mucosae and submucosa, consistent with secondary/extrinsic tumor involvement. The mucosa per se was within normal limits. Such a phenomenon has been previously reported [21].

Cystoscopic examination of signet ring-cell tumors often reveals no obvious mucosal or mass lesion. The mucosal surface is described as simply edematous, bullous, erythematous, or finely granular [4]. Erdogru et al. [3] cited 70 cases of such tumors that diffusely invaded the bladder wall without forming intraluminal growths. When a mass lesion was recognizable, it has been described as pedunculated, polypoid, sessile, and ulceroinfiltrative [4,22].

Treatment modalities currently available for such tumors are surgery, radiotherapy, and chemotherapy. Surgical options range from transurethral resection [6,22] and segmental cystectomy [3,6] to radical cystectomy with urinary diversion [6,23]. Small tumors detected early are amenable to transurethral resection [22]. However, since most present late, open surgery is usually required. Radiotherapy and chemotherapy alone have had limited success and are usually used as adjuvant therapy to surgery [3,4,22]. The high rate of recurrence of these tumors renders a thorough assessment of the pelvic area crucial with any chosen therapeutic modality. Should the tumor be deemed inoperable, palliative measures, including urinary diversion, need to be considered. With our case, the tumor burden proved to be unresectable as there was invasion of the rectum. Furthermore, the age and wishes of the patient dictated that no further aggressive therapy be attempted.

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